Title: Multivariate Prediction of Prostate Cancer in Puerto Rican and African American Men

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ABSTRACT

Important ethnic and racial differences exist in Prostate Cancer (PCA) epidemiology. PCA mortality is higher among both African American (AA) and Puerto Rican (PR) Hispanic men when compared with other Hispanic and Caucasian men in the United States.1-5 Among AA PCA patients molecular differences in the disease characteristics at the DNA, mRNA, and protein levels have been discovered and may play a role in disease aggressiveness.6-8 Both AA and PR populations are heterogeneous with respect to West African Ancestry (WAA), which is a risk factor for PCA incidence and (potentially) mortality.9-11 In fact, recent data from the Puerto Rican Cancer Registry show that many of the municipalities with the highest PCA mortality also have the greatest concentration of inhabitants of WAA.3,11 Therefore, one could postulate that increased mortality among PR men could be related to genetic admixture and specifically WAA. PCA is a complex disease; there is a need to study these two populations at increased risk for mortality in a comprehensive manner, integrating genetic markers of disease aggressiveness, WAA, environment interactions, influence of behaviors (exercise, smoking); socioeconomic status (SES), and comorbidities to determine if such variables enhance the prediction of PCA and its aggressiveness over standard clinical variables (i.e., serum prostate specific antigen [PSA] and digital rectal examination [DRE]). In our current project (Pilot Project E), we have accrued a cohort of both PR and AA prostate cancer cases and controls to begin to characterize the variables that contribute to both disease presence and the aggressive phenotype. The long-term goal of our research, which is carried forward in the renewal is to characterize features of PCA and its aggressive phenotype among at risk PR and AA men as a step toward decreasing PCA mortality among the two populations. The objective of our newly proposed study (Full Project A) is to design multivariable models to define key factors associated with the detection of PCA and its aggressive features in both high risk populations. Our hypotheses, derived in part from our preliminary data (see Preliminary Studies) is that: 1) specific genetic (i.e., WAA, and /or other PCA genetic polymorphisms) environmental, and lifestyle factors contribute to PCA incidence or virulence, and 2) an assessment of these variables could enhance the prediction of PCA or its behavior among our two high risk populations. These hypotheses will be tested in the following specific aims:

SPECIFIC AIMS

Aim 1: To establish and characterize a unique specimen/data repository for AA and PR men in two distinct studies: (a) Prospective collection of tissue, blood, urine, along with well annotated clinical, epidemiologic data among both cohorts undergoing prostate biopsy and (b) Expansion of our current retrospective cohort database of PR and AA PCA patients having undergone radical prostatectomy (RP).

Aim 2: To prospectively assess genotypic, clinical, pathologic, and epidemiologic data collected in Aim 1a and correlate the variables with the presence (or absence) and aggressiveness of PCA subsequent to biopsy among AA and PR patients. Our working hypothesis is that specific genetic (i.e., WAA, and /or other PCA genetic polymorphisms) environmental, and lifestyle factors contribute to PCA incidence or aggressive features and could enhance the prediction of PCA at biopsy among at risk populations.

Aim 3: To assess genotypic, clinical, pathologic, and epidemiologic data assessed in Aim 1b and correlate the variables with adverse pathologic features and disease recurrence among AA and PR patients. Our working hypothesis is that a higher proportion of WAA and/or PCA-associated polymorphisms will correlate with PCA aggressiveness and recurrence in both populations.

Based on the above, the outcomes from this research will contribute unique data to understand the multifactorial nature of the disease in two understudied populations with increased PCA mortality.